U.S. Army Environmental Hygiene Agency

TOPICAL HAZARD EVALUATION PROGRAM, ASSESSMENT OF THE RELATIVE TOXICITY OF CANDIDATE INSECT REPELLENTS

AI3-29853	AI3-38381
AI3-31658	AI3-38693
AI3-38097	AI3-39079
AI3-38232	AI3-39080
AI3-38348	AI3-39083
AI3-38378	AI3-54120

U.S. DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS STUDY NOS.

75-51-0650-91	75-51-0663-91
75-51-0651-91	75-51-0738-91
75-51-0654-91	75-51-0757-91
75-51-0655-91	75-51-0758-91
75-51-0656-91	75-51-0759-91
75-51-0661-91	75-51-0761-91

FEBRUARY 1992

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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-6422

REPLY TO
ATTENTION OF

EXECUTIVE SUMMARY
TOPICAL HAZARD EVALUATION PROGRAM, ASSESSMENT OF THE RELATIVE TOXICITY OF CANDIDATE INSECT REPELLENTS

1. PURPOSE. To provide guidance for further entomological testing of the subject insect repellents by means of laboratory toxicological studies. In addition, these data may be useful in developing preliminary safety guidelines for handling these compounds.

2. RECOMMENDATIONS.

a. Approve the following compounds for further entomological testing:

AI3-39079	AI3-38097
AI3-39083	AI3-29853
AI3-54120	AI3-38378
AI3-38232	AI3-38381
AI3-38348	AI3-38693

b. Conduct no further developmental studies on candidate repellents AI3-39080 and AI3-31658 due to their propensity for causing deleterious effects.

DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010-6422

REPLY TO
ATTENTION OF

HSHB-MO-T

TOPICAL HAZARD EVALUATION PROGRAM, ASSESSMENT OF THE RELATIVE TOXICITY OF CANDIDATE INSECT REPELLENTS

AI3-29853	AI3-38381
AI3-31658	AI3-38693
AI3-38097	AI3-39079
AI3-38232	AI3-39080
AI3-38348	AI3-39083
AI3-38378	AI3-54120

U.S. DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS STUDY NOS.

75-51-0650-91	75-51-0663-91
75-51-0651-91	75-51-0738-91
75-51-0654-91	75-51-0757-91
75-51-0655-91	75-51-0758-91
75-51-0656-91	75-51-0759-91
75-51-0661-91	75-51-0761-91

FEBRUARY 1992

1. REFERENCES.

a. Toxicology Division, Topical Hazard Evaluation Program (THEP) Procedural Guide, October 1985.

(1) Standing Operating Procedure (SOP) No. 8, U.S. Army Environmental Hygiene Agency (USAEHA), HSHB-MO-T, Primary Dermal Irritation Study.

(2) SOP No. 7, USAEHA, HSHB-MO-T, Primary Eye Irritation Study.

(3) SOP No. 12, USAEHA, HSHB-MO-T, Photochemical Skin Irritation Study.

(4) SOP No. 61, USAEHA, HSHB-MO-T, Guinea Pig Skin Sensitization Test (Buehler Technique).

Use of trademarked names does not imply endorsement by the U.S. Army but is intended only to assist in identification of a specific product.

Tox Eval Nos. 75-51-0650, 0651, 0654 through 0656, 0661, 0663, 0738, 0757, 0758, 0759, and 0761-91, Feb 92

b. Toxicity of Arthropod Repellents, Appraisal of the Armed Forces Topical Hazard Evaluation Program. Subcommittee on Arthropod Repellents, Committee on Toxicology, National Research Council. National Academy Press, Washington, DC, 1987.

2. AUTHORITY.

a. Letter, U.S. Department of Agriculture, Agricultural Research Service, Beltsville, Maryland, 14 November 1986, subject: Chemical Transmittal for THEP.

b. Letter, U.S. Department of Agriculture, Agricultural Research Service, Beltsville, Maryland, 18 December 1986, subject: Chemical Transmittal for THEP.

c. Letter, U.S. Department of Agriculture, Agricultural Research Service, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 18 August 1987, subject: Request Priority Testing.

d. Letter, U.S. Department of Agriculture, Agricultural Research Service, Beltsville, Maryland, 16 December 1987, subject: Chemical transmittal for THEP.

e. Memorandum of Understanding between the U.S. Army Health Services Command; the Department of The Army, Office of The Surgeon General; the Armed Forces Pest Management Board; and the U.S. Department of Agriculture, Agricultural Research, titled Biological and Toxicological Testing of Pesticides, effective 7 October 1987.

f. 40 CFR 156.10, Labeling Requirements, revised 1 July 1990.

g. Eye Effects: [EPA] PR Notice 81-3; Label Improvement Program: Change in Test Methods for and Categorization of Eye Irritation, 29 September 1981.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of candidate insect repellents; U.S. Department of Agriculture (USDA) proprietary chemicals.

4. MATERIALS.

a. Test Compounds. The 12 candidate insect repellents used in these studies were synthesized and provided by the Insect Chemical Ecology Laboratory, Agriculture Research Service, USDA, Beltsville, Maryland.

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b. Animals.*†

(1) Testing for primary skin irritation, photochemical skin irritation, and primary eye irritation was conducted using New Zealand White rabbits (2.8-4.5 kg) of either sex obtained from Hazelton-Dutchland Laboratories, Denver, Pennsylvania. Female Albino-Hartley guinea pigs (375-425 gm), also from Hazelton-Dutchland Laboratories, were used for sensitization studies and for determination of dermal toxicity. Male Sprague-Dawley rats (175-225 gm) from Charles River Laboratories, Wilmington, Massachusetts, were used for the oral toxicity studies. Quality control determinations made during a 2-week quarantine period showed the animals to be of acceptable health.

(2) Rabbits, guinea pigs, and rats were housed individually in wirebottom stainless steel cages. Drinking water and feed (Purina® Rabbit Chow 5322; Ziegler Rodent Ration 35-553 and Ziegler Certified Guinea Pig ration 35-564) were available ad libitum. Ambient temperatures in the animal rooms were maintained at 21 to 25 °C with relative humidity between 40-60 percent. The light/dark cycle was 12-hour intervals.

c. Contract Studies. Mutagenicity evaluation of the test substances was performed under commercial contract by Integrated Laboratory Systems (ILS), Research Triangle Park, North Carolina. The contract number was ILS Project No. 02200, DAAD05-88-M-M580.

5. METHODS.

a. Skin Irritation. An acute dermal irritation test, based upon the method of Draize, was conducted in rabbits. The procedure [reference 1a(1)] involved the single application of 0.5 gm or mL of each test substance to the clipped backs of six rabbits. The materials were held in contact with the skin under a gauze patch and overwrap of Coban® (occlusive). Exposure was

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* In conducting the studies described herein, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," U.S. Department of Health, Education and Welfare Publication No. (NIH) 85-23, 1985.

† The studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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® Coban is a registered tradename of 3M, St. Paul, Minnesota.

for 24 hours followed by scoring of irritation. Evaluations were also performed at 48 and 72 hours and at 7 days. Scoring of irritation was based on the Draize method in which erythema and edema were evaluated on a scale of 0 to 4 for severity. Categorizing the responses was based on the mean of the sum of the 24- and 72-hour scores.

b. Eye Irritation. Eye irritation studies were performed in rabbits following a standard method [reference 1a(2)]. A single 0.1 gm or mL dose of the test substance was administered to the conjunctival sac of each of six rabbits. Eyes were examined for gross signs of irritation at 24, 48, and 72 hours, and 7 days following exposure. Scoring of irritation effects followed the method of Draize in which the total score for the eye is the sum of all scores obtained for the cornea, iris, and conjunctiva. Categorizing the responses was based on the mean of the 24-hour evaluations.

c. Photochemical Skin Irritation. A photochemical skin irritation study was performed to assess the potential of the test substances to become chemically reactive when exposed to sunlight. Studies were performed [reference 1a(3)] by applying 0.05 mL of the test solution (25 percent in 95 percent ethanol) to the right side of the clipped backs of six rabbits. After 5 minutes the backs were exposed to ultraviolet (UV) light (365 nm) for 30 minutes at a distance of 10-15 cm. Following UV exposure of the rabbits, the left side of the same animal's back was treated identically to the right side, except that it was not irradiated. Oil of Bergamot, a known photoirritant, was included in the exposure regimen to assure the responsiveness of the test system. Photochemical irritation was evaluated at 24, 48, and 72 hours post-exposure. Scoring of erythema and edema was based upon the method of Draize.

d. Oral Toxicity. An approximate lethal dose (ALD) study, which uses a small number of animals, was performed to determine the minimum lethal dose of the test chemical. Single oral graded doses of technical grade material were given by gavage to male rats. Following administration of the test substance, animals were examined daily for onset of toxic signs. Animals surviving the 14-day observation period were sacrificed for gross pathological examination. The ALD of the test substance was considered to be the lowest dose that caused death during the 14-day observation period.

e. Sensitization. Sensitization studies were performed to determine the potential of the test substance for causing skin sensitization reactions in humans. The test procedure was based

on the method of Buehler [reference 1a(4)]. Technical grade test material was applied under Webril® patches to the shaved backs of 10 guinea pigs. Dinitrochlorobenzene, a known skin sensitizer, was included as a positive control. The occlusive exposure was for 6 hours, once per week, for 3 weeks. This was considered the "induction" phase. Following a 2-week rest period the animals were "challenged," meaning that a single application of the test material was applied to a naive site. Five other additional naive animals also received the challenge dose. Twenty-four and 48 hours after the challenge, the skin was depilated and irritation responses scored 3 hours later. The appearance of erythema and/or edema at the challenge site which was greater than that observed on the naive animals (no induction) was considered an allergic response.

f. In Vitro Mutagenicity Assays. The subject chemicals were evaluated for mutagenic activity in the Ames Salmonella/Microsome Plate assay. The Ames test used Salmonella typhimurium indicator strains TA-1535, TA-1537, TA-1538, TA-98, and TA-100. The assays were conducted in duplicate and in the presence and absence of metabolic activation. The assays were conducted at doses based on preliminary toxicity tests with the strain TA-100. For the actual assay, doses were selected with the highest dose exhibiting ≤ 90 percent toxicity and ranged over a series of five doses, from 5 µL/plate to 30 µL/plate.

g. The USAEHA and the U.S. Environmental Protection Agency (EPA) hazard indicator indexes (Appendices A, B, and C) were used when applicable to place the results from the various tests into various toxicity categories.

6. RESULTS.

a. Skin Irritation. A tabular presentation of the skin irritation data for each test substance appears in Table 1.

b. Eye Irritation. A tabular presentation of the eye irritation data appears in Table 2.

c. Photochemical Irritation. A tabular presentation of the photochemical irritation data appears in Table 3.

d. Oral Toxicity. A tabular presentation of the oral toxicity data appears in Table 4.

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TABLE 1. SKIN IRRITATION

Substance	Study No.	Results	Category USAEHA	Category EPA
AI3-39079	75-51-0650	Mild irritation with scores from 2 to 0 with a mode of 0	II	III
AI3-39083	75-51-0651	Mild irritation with scores from 2 to 0 with a mode of 1	I	IV
AI3-54120	75-51-0654	Very slight irritation with scores from 1 to 0 with a mode of 0	I	IV
AI3-38232	75-51-0655	Marginal irritation with scores from 2 to 0 with a mode of 0	I	IV
AI3-39080	75-51-0656	Mild irritation with scores of 1 to 0 with a mode of 0	II	III
AI3-38348	75-51-0661	Very slight irritation with scores of 1 to 0 with a mode of 0	I	IV
AI3-38097	75-51-0663	Very slight irritation with scores of 1 to 0 with a mode of 0	II	IV
AI3-29853	75-51-0738	Mild irritation with scores from 2 to 0 with a mode of 0	II	IV
AI3-31658	75-51-0757	Slight irritation with score from 2 to 0 with a mode of 0	I	IV
AI3-38378	75-51-0758	Very slight irritation with scores from 1 to 0 with a mode of 0	I	IV
AI3-38381	75-51-0759	Very slight irritation with scores from 1 to 0 with a mode of 0	I	IV

TABLE 2. EYE IRRITATION

Substance	Study No.	Results	Category USAEHA	Category EPA
AI3-39079	75-51-0650	No effects on the eye	A	IV
AI3-39083	75-51-0651	No effects on the eye	A	IV
AI3-54120	75-51-0654	Mild corneal opacity and moderate conjunctival irritation resolved by day 7	E	III
AI3-38232	75-51-0655	Mild corneal opacity and slight conjunctival irritation resolved by day 7	E	III
AI3-39080	75-51-0656	Slight corneal opacity and slight conjunctivae irritation	A	IV
AI3-38348	75-51-0661	Mild to moderate corneal opacity and irritation to the conjunctivae cleared by 14 days	E	II
AI3-38097	75-51-0663	Mild corneal opacity with iritis and moderate to conjunctivae irritation cleared by 7 days	E	III
AI3-29853	75-51-0738	Mild corneal opacity and slight conjunctivae irritation cleared by 14 days	C	II
AI3-31658	75-51-0757	Moderate corneal opacity with mild irritation to the conjunctivae	C	III
AI3-38378	75-51-0758	No effects on the eye	A	IV
AI3-38381	75-51-0759	No effects on the eye	A	IV
AI3-38693	75-51-0761	Moderate corneal opacity and irritation to the conjunctivae, Cleared by 7 days	C	III

Tox Eval Nos. 75-51-0650, 0651, 0654 through 0656, 0661, 0663, 0738, 0757, 0758, 0759, and 0761-91, Feb 92

TABLE 3. PHOTOCHEMICAL IRRITATION

Substance	Study No.	Results
AI3-39079	75-51-0650	No photochemical irritation
AI3-39083	75-51-0651	No photochemical irritation
AI3-54120	75-51-0654	No photochemical irritation
AI3-38232	75-51-0655	No photochemical irritation
AI3-39080	75-51-0656	No photochemical irritation 25% alcohol solution caused a slight irritant response
AI3-38348	75-51-0661	No photochemical irritation
AI3-38097	75-51-0663	No photochemical irritation
AI3-29853	75-51-0738	No photochemical irritation
AI3-31658	75-51-0757	Very strong irritant response to ethanol solutions
AI3-38378	75-51-0758	No photochemical irritation
AI3-38381	75-51-0759	No photochemical irritation
AI3-38693	75-51-0761	No photochemical irritation

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TABLE 4. ORAL TOXICITY - ALD RATS

Substance	Study No.	Approximate Lethal Dose	Signs	Category EPA
AI3-39079	75-51-0650	>3333 mg/kg	ruffled pelt	III
AI3-39083	75-51-0651	>3333 mg/kg	ruffled pelt	III
AI3-54120	75-51-0654	2222 mg/kg	salivation	III
AI3-38232	75-51-0655	>3333 mg/kg	ataxia, prostration	III
AI3-39080	75-51-0656	>3333 mg/kg	transient lethargy	III
AI3-38348	75-51-0661	987 mg/kg	excessive salivation lethargy	III
AI3-38097	75-51-0663	>3333 mg/kg	no signs	III
AI3-29853	75-51-0738	2222 mg/kg	ataxia	III
AI3-31658	75-51-0757	Not Performed	---	-
AI3-38378	75-51-0758	>5000 mg/kg	no signs	IV
AI3-38381	75-51-0759	>5000 mg/kg	no signs	IV
AI3-38693	75-51-0761	1400 mg/kg	sl ataxia	II

e. Skin Sensitization. A tabular presentation of the skin sensitization data appears in Table 5.

f. Mutagenicity. The Ames test results appear in Table 6.

7. DISCUSSION.

a. The purpose of the THEP is to investigate relevant health end points of proposed repellent chemicals. Data from these studies are used to recommend the course of further entomological and toxicological evaluations with the subject chemical.

b. The results from the acute skin irritation studies showed that none of the compounds tested as technical grade agents produced skin responses that would cause a recommendation for disapproval. However, an ethanol solution of AI3-31658 in the photochemical test caused a strong skin irritant response while an ethanol solution of AI3-39080 was slightly irritating to the skin. In addition, AI3-39080 was a potential sensitizing agent. These findings are considered to be a basis for rejecting a candidate repellent for further entomological and toxicological development.

c. The results of the eye irritation tests showed that three compounds produced significant irritation resulting in a USAEHA Category E classification that would serve as a basis for rejection. However, this finding is no longer considered a basis for rejection if the irritation response is resolved within 7-14 days. Further eye irritation testing is indicated at proposed use concentrations with the three candidate repellents as their development progress to step 5, advanced toxicology.

d. The results of the Ames tests for mutagenicity showed only intermittent scattered positive responses for the 11 compounds tested. The responses were generally weak and not dose response related within and between the indicator strains. Additional mutagenicity assays would be performed on those candidate repellents progressing to step 5 of testing.

8. RECOMMENDATIONS.

a. Disapprove candidate repellents AI3-31658 and AI3-39080 for further entomological testing based upon their demonstrated adverse toxicological effects.

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TABLE 5. SKIN SENSITIZATION

Substance	Study No.	Results
AI3-39079	75-51-0650	No sensitization reaction
AI3-39083	75-51-0651	No sensitization reaction
AI3-54120	75-51-0654	No sensitization reaction
AI3-38232	75-51-0655	No sensitization reaction
AI3-39080	75-51-0656	Some sensitization reactions
AI3-38348	75-51-0661	No sensitization reaction
AI3-38097	75-51-0663	No sensitization reaction
AI3-29853	75-51-0738	No sensitization reaction
AI3-31658	75-51-0757	No sensitization reaction
AI3-38378	75-51-0758	No sensitization reaction
AI3-38381	75-51-0759	No sensitization reaction
AI3-38693	75-51-0761	No sensitization reaction

Tox Eval Nos. 75-51-0650, 0651, 0654 through 0656, 0661, 0663, 0738, 0757, 0758, 0759, and 0761-91, Feb 92

TABLE 6. MUTAGENICITY - AMES TEST

Substance	Study Number		Indicator Strains TA1535	TA1537	TA1538	TA98	TA100
AI3-39079	75-51-0650	Act	-	-	-	-	-
		Nonact	-	-	-	-	-
AI3-39083	75-51-0651	Act	-	-	-	-	-
		Nonact	-	-	-	-	-
AI3-54120	75-51-0654	Act	-	-	-	-	-
		Nonact	-	-	-	-	-
AI3-38232	75-51-0655	Act	-	-	-	-	-
		Nonact	-	+	-	-	-
AI3-39080	75-51-0656	Act	-	-	+	-	-
		Nonact	-	-	-	-	-
AI3-38348	75-51-0661	Act	-	-	-	-	-
		Nonact	+	-	-	-	-
AI3-38097	75-51-0663	Act	-	-	-	-	-
		Nonact	+	-	-	-	-
AI3-29853	75-51-0738	Act	not performed				
		Nonact	not performed				
AI3-31658	75-51-0757	Act	-	-	-	-	-
		Nonact	-	-	-	-	-
AI3-38378	75-51-0758	Act	-	+	-	-	-
		Nonact	-	-	-	-	-
AI3-38381	75-51-0759	Act	-	+	-	-	-
		Nonact	-	-	-	-	-
AI3-38693	75-51-0761	Act	-	-	-	-	-
		Nonact	-	-	-	-	-

- negative mutagenic activity
+ weak positive response
act - activated
nonact - nonactivated

Tox Eval Nos. 75-51-0650, 0651, 0654 through 0656, 0661, 0663, 0738, 0757, 0758, 0759, and 0761-91, Feb 92

b. Approve the following candidate repellents for further entomological testing:

AI3-39079
AI3-39083
AI3-54020
AI3-38232
AI3-38348
AI3-38097
AI3-29853
AI3-38378
AI3-38381
AI3-38693

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APPENDIX A

USAEHA CATEGORIES FOR SKIN IRRITATION EFFECTS

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. Score Limits: Intact 0-0.5; Abraded 0.51-2.0; Total 0-2.0 (INTERPRETATION: No restriction for acute application to the human skin).

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. Score Limits: Intact >0.5; Total 0.51-2.0 (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as clothing impregnant).

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. Score Limits: Total 2.1-5.0 (INTERPRETATION: Should not be used directly without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals).

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion. Score Limits: Total 2.1-7.9 (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing inhumans, at concentrations which have been shown not to produce primary irritation in animals).

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound or compounds producing necrosis, vesiculation, or eschars. Score Limits: Total 8.0 or not scorable (INTERPRETATION: Not suitable for use on humans).

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APPENDIX B

EPA - TOXICITY CATEGORY CRITERIA

Hazard Indicators	Category I	Category II	Category III	Category IV
Oral LD50	Up to and incl 50 mg/kg	>50 thru 500 mg/kg	>500 thru 5000 mg/kg	>5000 mg/kg
Dermal LD50	Up to and incl 200 mg/kg	>200 thru 2000 mg/kg	>2000 thru 20,000 mg/kg	>20,000 mg/kg
Inhal LC50 (Chmbr conc)	Up to and incl 0.2 mg/L	<0.2 thru 2.0 mg/L	>2.0 thru 20 mg/L	>20 mg/L
Eye Effects	Corrosive (Irrevers de-struc of ocular tiss) or corneal involv or irrit persist for more than 21 days	Corneal involv or irrit clrng in 8-21 days	Corneal involv or irrit clrng in 7 days or less	Min effects clrng in less than 24 hrs
Skin Effects	Corrosive (Tiss destruc into dermis and/or scarring)	Sev irrit at 72 hrs (sev erythema or edema)	Mod irrit at 72 hrs (mod erythema)	Mild or slt irrit (no irrit or slt erythema)

References:

40 CFR 156.10, Labeling Requirements, revised 1 July 1990.

Eye Effects: [EPA] PR Notice 81-3; Label Improvement Program: Change in Test Methods for and Categorization of Eye Irritation, 29 September 1981.

Tox Eval Nos. 75-51-0650, 0651, 0654 through 0656, 0661, 0663, 0738, 0757, 0758, 0759, and 0761-91, Feb 92

APPENDIX C

USAEHA CATEGORIES FOR EYE IRRITATION EFFECTS

CATEGORY A - Compounds noninjurious to the eye. Score Limits: 0-10 (individual conjunctival score for chemosis, redness or discharge not to exceed 1). (INTERPRETATION: Irritation of human eyes is not expected if the compound should accidently get into the eyes, provided it is washed out as soon as possible.)

CATEGORY B - Compounds producing mild injury to the cornea. Score Limits: 10-20 (individual conjunctival score for chemosis, redness or discharge not to exceed 1). (INTERPRETATION: To be used with caution around the eyes.)

CATEGORY C - Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. Score Limits: 5-30 (individual conjunctival score for chemosis, redness or discharge exceed 1). [INTERPRETATION: To be used with caution around the eyes and mucosa (e.g., nose and mouth).]

CATEGORY D - Compounds producing moderate injury to the cornea. Score Limits: <20-50 (individual conjunctival score for chemosis, redness or discharge not to exceed 1). (INTERPRETATION: To be used with extreme caution around the eyes.)

CATEGORY E - Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctival. Score Limits: 20-50 (individual conjunctival score for chemosis, redness or discharge exceed 1). (INTERPRETATION: To be used with extreme caution around the eyes and mucosa.)

CATEGORY F - Compounds producing severe injury to the cornea and to the conjunctiva. Score Limits: 50 or greater. (INTERPRETATION: To be used only with extreme caution; it is recommended that use be restricted to areas other than the face.)